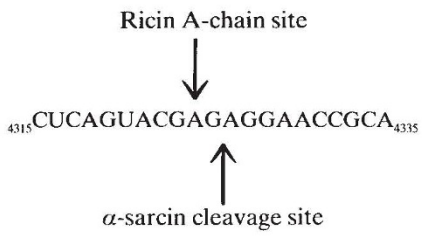


Ricin A-chain removes adenine from A_{4324} located close to the α-sarcin cleavage site in a highly conserved region near the 3′ end of 28S RNA. Subscript numbers indicate the position of the bases in the sequence, counted from the 5′ end. The total length of 28S RNA from rat liver is 4,813 nucleotides.

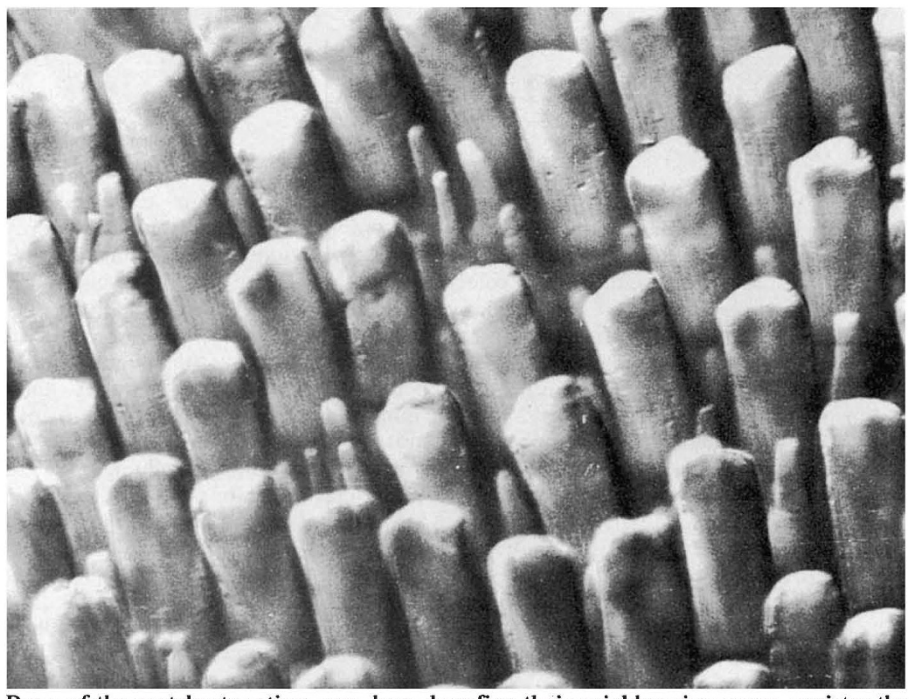
ricin A-chain was never demonstrated convincingly.

Endo and colleagues[2,3] also searched in vain for an RNase activity associated with ricin. But, unlike previous workers, they noticed an almost undetectable reduction in the electrophoretic migration rate of 28S RNA from ricin-treated ribosomes. A 550-nucleotide fragment derived from the 3′ end of the 28S RNA migrates slightly more slowly than the corresponding fragment from untreated ribosomes. Their subsequent analysis of the 550-nucleotide fragment allowed them to elucidate the mechanism of enzymatic action of the ricin A-chain.

In 28S from ricin-treated ribosomes, adenine is missing from position A_{4324} although the phosphoribose backbone is left intact (see figure). This renders the bond between G_{4323} and A_{4324} nuclease-resistant, whereas the phosphodiester bonds on both sides of A_{4324} become hypersensitive to cleavage by alkali and by anilin at low *p*H. Interestingly, A_{4324} lies in a region that is strongly conserved between species.

Endo *et al.* in their new work also show that ricin removes close to one adenine residue per ribosome, indicating that A_{4324} is the sole site of action. Intact ribosomes and 60S subunits are the most sensitive substrates, but native 28S RNA is also modified, although at a reduced rate. On the other hand, denatured 28S RNA and the 550-nucleotide fragment are resistant. Apparently, ricin A-chain recognizes the three-dimensional structure around A_{4324}. Consistent with this observation, *Escherichia coli* ribosomes, which also contain the conserved sequence, are resistant to the enzymatic activity of ricin A-chain[3], and the toxin does not inhibit their action.

Several plant toxins have a similar structure and action to ricin. Endo *et al.* found that two of these, abrin and modeccin, remove adenine from A_{4324}. They also found the same enzymatic activity in pokeweed antiviral protein, a member of a large group of A-chain-like proteins. These proteins inactivate ribosomes in cell-free systems, but because they lack a B-chain, are not toxic to intact cells. A-chain-like proteins are present in high amounts in a vast number of plants, including such familiar species as wheat and carnation[4], but their function is not understood.



Rods of the vertebrate retina, seen here dwarfing their neighbouring cones, register the capture of photons by changing their membrane voltage. This signal is passed to higher-order visual neurons through a chemical synapse, and to adjacent photoreeceptors through electrical synapses. On page 522 of this issue, D. Attwell, S. Borges, S. Wu and M. Wilson report the surprising finding that only signals in the first one-fifth of the voltage response range of the rods are actually transmitted across the chemical synapse, and larger signals are clipped. The authors suggest that the electrical synapses between photoreceptors help to avoid this clipping, by allowing light to produce a small signal in many photoreceptors, each of which has its chemical synapse operating at a high gain. The average diameter of the top of a rod is 11.5 μm. □

Although the cytotoxin from the bacterium *Shigella dysenteriae* was known to inactivate catalytically the 60S ribosomal subunit[5], it came as a surprise that this bacterial toxin acts like ricin in that it removes adenine from A_{4324} (ref. 3). Closely related toxins (Shiga-like toxins) are produced by several enteropathogenic bacteria and one such toxin, which has recently been sequenced[6], shows marked homologies to ricin A-chain. Possibly, therefore, the bacteria have picked up a common plant gene for their own malevolent purposes.

A major problem that remains to be solved is how ricin crosses the cell membrane to reach its targets in the cytosol. Endocytic uptake must be involved, but transfer to the cytosol seems to come from a compartment distal to endosomes. Ultrastructural and biochemical data have focused attention on the trans-Golgi network as the possible transfer site[7,8]. Ingenious experiments recently published by Youle and Colombatti[9] support this possibility. These authors tested the ricin sensitivity of hybridoma cell lines that produce anti-ricin antibodies. On their way to the surface the antibodies, like other export proteins, pass through the trans-Golgi network where they can meet endocytosed ricin. These hybridoma cells are highly resistant to ricin, and appropriate controls exclude the possibility that antibodies in the medium or at the cell surface cause the resistance.

Considerable progess has also been made in the elucidation of ricin structure. The toxin had earlier been sequenced and cloned, but now the three-dimensional structure has been solved at 2.8-Å resolution[10] and data at 2.4-Å resolution are expected soon. The penetration process can therefore now be probed by site-directed mutagenesis of selected regions of the toxin. □

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